Overview of FDA's Animal Feed Safety System

July 2014

Purpose and Scope: The Food and Drug Administration's (FDA's) Center for Veterinary Medicine (CVM) has cataloged – under the Animal Feed Safety System (AFSS) – the laws, regulations, major initiatives, and policies related to animal feed safety.

The AFSS covers the entire continuum of Agency animal feed activities, including:

- pre-approving additives for use in feed;
- establishing limits on feed hazards;
- providing education and training;
- conducting research;
- performing inspections and investigations;
- taking enforcement actions for ensuring the removal of unsafe feed from the marketplace and compliance with Agency regulations; and,
- establishing partnerships with other agencies with responsibility for feed safety.

The AFSS includes regulations and guidance pertaining to…

- manufacture
- labeling
- storage
- distribution and
- use

…of **all** feed at **all** stages, from manufacture to use, whether at commercial or non-commercial feed establishments, farms where animals are raised, and homes where pet animals are kept.

This document provides an update of the most recent activities aimed at filling gaps and addressing shortcomings of the current safe feed regulatory structure, as identified by the AFSS Team. This document provides an overview of all the elements that make up FDA's AFSS.

Background

FDA has regulated the safety of feed since 1906, when the Pure Food and Drug Act was passed. Provisions of the 1906 Act were incorporated into the Federal Food, Drug, and Cosmetic Act (FDCA), which was passed in 1938 and became the basic Federal statute giving FDA the authority to regulate food, including food for animals (animal feed and pet food) and drugs for humans and animals.

Historically, FDA's feed program has focused on specific safety issues – unsafe tissue residues resulting from feeding of medicated feeds, Bovine Spongiform Encephalopathy (BSE), *Salmonella*, and unsafe food additives, for instance. But it did not address feed

safety in a comprehensive manner. The AFSS was initiated to develop a comprehensive feed safety program to help identify feed hazards and their potential sources. The AFSS is also designed to enable establishments and FDA to prevent or eliminate the occurrence of unacceptable feed risks from those hazards.

FDA is not the only government entity overseeing the safety of animal feed. FDA works with States, some through formal agreements, and some on a more informal basis, to ensure compliance with Federal regulations. States also have their own programs that complement FDA's efforts. The State programs are aimed at ensuring that feeds do not cause health problems in animals and do not lead to unsafe human food derived from animals. Also, the State programs help to ensure feeds that are nutritionally adequate for their intended species. In addition to feed safety programs, States have other programs to minimize economic losses for feed purchasers, such as programs ensuring that feed products meet label guarantees for nutritional components.

States work cooperatively through the Association of American Feed Control Officials (AAFCO). AAFCO membership includes State feed offices, FDA, the Canadian Food Inspection Agency, Puerto Rico and Costa Rica. One of AAFCO's major objectives since its inception in 1909 is establishing uniform regulations applying to animal feed through the development of model regulations and policies. Another major AAFCO objective is to provide a forum whereby feed industry representatives and government regulators can identify, discuss, and resolve feed regulatory issues. Yearly, AAFCO publishes an updated version of its *Official Publication*, which contains proceedings from meetings, definitions of feed terms, official names and definitions for feed ingredients, and model regulations.

Reason for AFSS: Animal feed ingredients and mixed feeds produced and used in the United States have a good safety record. However, because government and industry attention has been limited and focused on known safety issues, potential human and animal health problems sometimes are hidden.

For example, in 1997 U.S. officials found high levels of dioxin in poultry, which ultimately was traced to dioxins present in ball clay, an anti-caking agent used in animal feed. Then in 2002, an overseas government discovered high levels of dioxin in a mineral product for animal feed imported from the United States. It turned out that the dioxin was a result of the high temperatures used in the mineral manufacturing process. High levels of dioxins in mineral supplements for feed reflect these types of hidden risks. Likewise, the public became alarmed in 2007 when imported feed ingredients contaminated with melamine and related compounds were used in pet food that sickened dogs and cats. Other animal food problems that have become issues in international markets are BSE, Chronic Wasting Disease, and microbial contamination.

The production and distribution of feed ingredients and mixed feed, and the marketing of meat, milk, and eggs derived from animals that consume these feed materials, have become global businesses. World markets, and the customers served by these markets,

react negatively when questions arise about the safety of a feed commodity introduced into domestic or international markets.

Implementation of a preventive, risk-based system comprised of both required (through regulation) and voluntary components, designed to ensure the continued production of safe feed, will help maintain user confidence about the safety of U.S. feed and animal-derived food supplies.

Focus on Food Safety

Since 2007 and 2008, when outbreaks of illness associated with both human food (spinach, tomatoes, cantaloupe, and peanut butter) and animal food (contamination of pet food by melamine and related chemicals) increased our focus on food safety, the U.S. government has developed a number of initiatives, all giving high priority to prevention, intervention, and improved response. The three most significant initiatives for animal food are the Food and Drug Administration Amendments Act of 2007 (FDAAA), the Food Safety Modernization Act of 2010 (FSMA), and the development of an Integrated Food Safety System (IFSS).

FDAAA: Provisions under Title X of FDAAA impose several food safety requirements on the FDA. Several of those requirements were in response to the dog and cat illness and death in the United States from pet food contaminated with ingredients containing melamine, cyanuric acid, and related compounds. FDAAA required FDA to establish an early warning system about unsafe pet food, develop new labeling for pet food, and set standards for pet food ingredients. FDAAA's requirements that apply to animal feed have been added to the developmental work identified in this document to ensure a comprehensive and preventive animal feed safety program.

FSMA: This Act, signed into law in January 2011, extensively changes the way FDA addresses human and animal food safety by placing an emphasis on prevention rather than reacting to a problem. FSMA gives FDA the legislative mandate to require comprehensive, science-based preventive controls across the food supply, including preventive controls for animal feed.

FSMA institutes a required frequency for FDA inspection and provides FDA with new enforcement authorities – such as mandatory recall authority, food safety records access, suspension of registration, and administrative detention – designed to achieve higher rates of compliance.

FSMA also provides FDA authority to ensure that imported products meet U.S. standards and are safe for U.S. consumers. Under FSMA, importers have an explicit responsibility to verify that their foreign suppliers have adequate preventive controls to ensure the safety of the food they produce. New programs, such as Voluntary Qualified Importer Program and Third-Party Certification, are being implemented as part of the FSMA imports provisions.

To implement FSMA's preventive control provisions for animal feed, FDA has proposed a regulation calling for Current Good Manufacturing Practice and Hazard Analysis and Risk-Based Preventive Controls for Food for Animals. The proposed rule applies to the manufacture of all animal feed, including pet food. It would require all domestic and foreign facilities that are already required to register under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 section of the FDCA to also implement current Good Manufacturing Practices for manufacturing, processing, packing, and holding animal feed. FDA will give the industry time to prepare for implementation of the Good Manufacturing Practice rules.

In addition, any facility covered by the FSMA regulation would be required to conduct an analysis of likely hazards it could face, and implement risk-based preventive controls to address those possible hazards. Several types of firms would be exempted from the proposed rule. For more information on the exemptions, go to the FSMA portion of the FDA Website (www.fda.gov/fsma).

FDA is committed to implementing the requirements through an open process with opportunity for input from all stakeholders. For additional information on FSMA, please visit: www.fda.gov/fsma.

IFSS: Federal, State, Local, Tribal, and Territorial regulatory and public health agencies (partner agencies) each have a role and responsibility for food safety in the United States. Partner agencies have worked together to help each other fulfill our food safety and public health mission for many years.

FSMA provided FDA with specific authority to enhance partnerships among partner agencies and provided a legislative backing to continue efforts to build the IFSS.

The ultimate goal of a national IFSS is mutual reliance, with seamless coordination and communication among partner agencies to ensure high rates of compliance with food safety laws and regulations. An IFSS also actively solicits input and support from industry, academia, and interested consumer groups. The Partnership for Food Protection has been tasked with continuing to develop and implement a national IFSS. The Partnership for Food Protection is a group of dedicated professionals from partner agencies with roles in protecting the food supply and public health. To learn more about the Partnership for Food Protection's vision for an IFSS, please visit: http://www.fda.gov/ForFederalStateandLocalOfficials/FoodSafetySystem/PartnershipforFoodProtection/default.htm.

Risk-Based Inspection Programs

Although facility inspection is an important element of an effective regulatory program, FDA does not have the resources to frequently inspect each feed and feed ingredient producer, distributor, or animal feeder, especially considering the size of the industry and the amount of feed that is produced and fed within just a few days. Instead, a risk-based

approach is required to identify which feed products, processes, and establishments present the greatest risk to animal and human health.

The Agency established priorities for inspections under the BSE program, starting in FY 2009, using a mathematically modeled, risk-based approach. This approach was originally developed in FY 2008 for inspection of FDA-licensed medicated feed mills for compliance with medicated feed current Good Manufacturing Practices and other Agency regulations. CVM is currently in the process of implementing a risk-based approach for feed-related inspections, which will allow the Center to prioritize inspections for a given fiscal year or other time frame and will permit the Center to identify specific establishments or types of establishments to be inspected. Statistically based audits will be conducted of establishments, or establishment types, not of high enough risk to warrant a full inspection, to assure the Agency that they were correctly categorized and to monitor for changes in industry practices.

A risk-based, preventive animal feed safety program requires feed producers and distributors to take into consideration hazards that could cause the feed to be unsafe, and to develop and implement a plan to prevent hazards from occurring. As such, feed producers should improve their ability to identify and minimize or eliminate hazards associated with animal feed before those hazards result in decreased animal productivity, adverse health consequences to the animals, and potential risks to human health. Also, animal feed producers who understand their own business and technical processes well enough to establish effective control points for naturally occurring or accidental feed hazards are also likely to be more capable of detecting and controlling deliberately introduced feed hazards.

FDA and State resources available for use in enforcement programs are limited, but can be more effectively utilized by focusing research, inspections, and feed sampling and analysis programs on those situations representing the greatest risks to animal health and the public. Also, we believe a more effective overall prevention-oriented feed safety program will lead to fewer resource-draining feed emergencies for government agencies.

Operating Principles of the AFSS

As the AFSS Team developed the program, it identified these operating principles as forming the basis for the AFSS:

1. The Federal and State regulatory agencies provide the rules, guidance, and oversight to assist industry in producing and distributing safe feed ingredients and mixed feed;
2. The feed and animal production industries are responsible for the production, distribution, and use of safe feed;
3. Rules and guidance provide flexibility in the approaches individual producers of feed can use to meet acceptable safety criteria;
4. Federal and State regulatory agencies cooperate on all aspects of feed regulation;

5. Federal and State feed regulatory agencies conduct inspections of feed-manufacturing establishments, review product labels, sample and analyze feed for feed hazards and for compliance with label guarantees, and take appropriate actions to address violations;
6. FDA uses risk-based decision-making to help determine which feed hazards should receive the highest priority by the Agency, and the best methods for addressing them;
7. FDA directs its regulatory resources to those feed hazards that pose the greatest risks to animal and public health;
8. Feed defense measures as they relate to preventing and responding to intentional acts of feed contamination are part of the AFSS;
9. Training is critical for ensuring that industry and regulatory agencies have the most up-to-date knowledge about FDA rules and guidance, and that enforcement by FDA and States is consistent and that it is conducted in an appropriate manner;
10. Feed intended for non-food producing animals, such as pets, is included along with feed for food-producing animals; and
11. Feed establishments covered by the AFSS include all facilities, equipment, and conveyances involved in the production, packaging, storage, and distribution of individual feed ingredients and mixed feed, and the feeding of animals.

Major Components of the AFSS and Key Definitions

Seven operating components (labeled A through G) comprise the AFSS. These components cover the processes used by FDA to ensure that:

- Ingredients used in feed are safe (components A and B);
- The methods used to make, store, and distribute feed result in safe products (component C);
- The Agency acquires timely information about unsafe feed and, when appropriate, makes such information publicly available (component D);
- The levels of regulatory oversight are commensurate with risk to human and animal health (component E);
- Training, education, and outreach activities keep our partners and stakeholders well informed and ensure that FDA and State feed regulatory personnel are adequately trained (component F); and
- An active and aggressive research program is employed to generate data to aid in addressing feed safety issues (component G).

More information on each component follows, including the identification of work in progress to strengthen the ability of the Agency to ensure that its regulatory program is effective and efficient and to help the industry ensure that its feed products are safe. The identified work in progress does not reflect all the steps the Agency is taking to improve its feed safety program; however, the identified work does present the more important actions.

A feed hazard is defined as a biological, chemical, radiological, or physical agent in feed with the potential to cause illness or injury to animals or humans. One regulatory challenge is defining terms in a way that takes into account the fact that the presence of certain agents in feed does not always pose a likely risk to animal or human health. It is when controls are not adequate at feed establishments that these same agents may cause the feed to be a much greater risk to animal or human health. For example, shipments of corn containing aflatoxins at levels below 0.1 parts per billion (ppb) are not likely to cause an adverse health consequence for animals given feed made with this corn or for people consuming the food derived from these animals. However, if environmental or other pertinent conditions are not controlled while the corn is in storage at the feed establishment and aflatoxin levels in corn rise above 20 ppb, then the feed establishment's use of this corn to make feed for lactating dairy cattle causes a much greater risk to health for people consuming milk products from these animals. The goal of AFSS is to eliminate or control a feed hazard so that it does not become a significant risk of causing illness or injury to animals or humans.

For this document, a commercial establishment is defined as an establishment (or individual) that sells, barters, trades, gives, donates, or debits a feed product. A non-commercial feed establishment is defined as a feed establishment (or individual) that does not sell or debit feed products (i.e., has no customers). Generally, a "farm" is a commercial feed establishment if any feed product produced on or by the farm is not used on the farm.

Also, in this document, the definition of feed includes feed ingredients and mixed feed intended for food-producing or other types of animals.

Component A – Ingredients and the Approval Process

The primary purpose of feed is to provide nutrients. In addition, other ingredients and additives are incorporated into feed, for example, to add color to the animal feed or the human food product, to ensure stability for nutrients, to provide flavor, and to prevent mold growth. Drugs may also be incorporated into feed for disease prevention and treatment, as well as for improved animal productivity. The FDCA provides the authority to FDA to regulate ingredients and additives used in feed.[*] Depending on its intended purpose, an ingredient or additive could be classified as a food additive, a new animal drug, or a color additive. Regulations that mandate and specify data requirements and the application or petition format required to be submitted for Agency review and approval for food additives, new animal drugs, and color additives are contained in Title 21 of the *Code of Federal Regulations* (CFR). These regulations also provide timeframes for Agency decisions on these applications/petitions.

FDA also controls some ingredients and additives by using procedures not presently covered by regulations. One example is the voluntary consultation process for plants

[*] Some articles added to feed fall under the purview of other Federal agencies. Feed-through pesticides are regulated by the Environmental Protection Agency, and vaccines added to feed are the responsibility of the U.S. Department of Agriculture.

modified through biotechnology. It is used to review data on the plants before the company introduces the modified plants into the marketplace.

Another example is the Generally Recognized as Safe (GRAS) Program for substances used in animal feed. The program was announced in the June 4, 2010, *Federal Register* (75 FR 31800-31803) initially as a pilot program (http://www.fda.gov/AnimalVeterinary/Products/AnimalFoodFeeds/GenerallyRecognizedasSafeGRASNotifications/ucm192219.htm). Under the program, after reviewing a notice submitted by a notifier, the FDA will inform the notifier that the Agency either has currently no questions about the notifier's determination that the substance is GRAS for its intended use, or that the FDA has identified issues that call into question the GRAS status of the ingredient.

A third example is the recognition by FDA of the names of feed ingredients defined in the AAFCO *Official Publication* as the common or usual name of the ingredients (see Compliance Policy Guide [CPG] 665.100, at http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074687.htm.

All FDA-approved food additives and color additives for use in animal feed are listed in 21 CFR 573, and 21 CFR 73, respectively. FDA lists substances it consider GRAS at 21 CFR 582 and 21 CFR 584. However, the Agency notes that it is impracticable to list all GRAS substances. The *Official Publication* of AAFCO provides a description of feed ingredients and additives. The *Official Publication* is updated on an annual basis to incorporate substance descriptions additions, modifications, or deletions, based on reviews completed by AAFCO members.

A few years ago, FDA developed a Memorandum of Understanding (MOU) with AAFCO explaining the roles of each organization in AAFCO's process for adding or modifying feed ingredient definitions in the Official Publication. The MOU is available at http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/DomesticMOUs/ucm115778.htm.

A complete listing of the formal and informal processes used by FDA and the location of ingredient/additive listings is provided in Appendix I.

Current Project Work:

Project A1. As required by the FDAAA, FDA will be establishing feed ingredient standards and definitions through the comment and rulemaking process. FDA established a docket (FDA-2007-N-0442) in a Federal Register notice on January 7, 2008, for receiving comments from its stakeholders on section 1002(a) of the FDAAA. In addition, a public meeting was held on May 13, 2008, in Gaithersburg, MD, at which the Agency received oral and written comments on the mandate from Congress to write regulations to

ensure pet food safety. FDA is drafting a regulation to fulfill the mandate to establish standards and definitions.

Project A2. FDA plans to write final regulations for accepting GRAS Notices for feed ingredients, which would transform the current pilot program into an official regulatory program. The Ingredient Safety Team has been established in CVM's Division of Animal Feeds to implement the GRAS Notification program. Sixteen GRAS notices have been submitted since the program started in 2010.

Project A3. CVM is taking steps to address concerns about the development of resistance in antimicrobial drugs important for human health stemming from the use of those drugs in food-producing animals, including drugs used in animal feeds. In FY 2010, CVM released for comment draft *Guidance for Industry #209, Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals*. This guidance was finalized in April 2012. It provides a framework for policy regarding the appropriate or judicious use of medically important antimicrobial drugs in food-producing animals and is based on available scientific information. The regulatory framework presented in the guidance includes phasing-in measures to limit use of medically important antimicrobial drugs in food-producing animals to those considered necessary to protect animal health. In addition, the regulatory framework would limit the use of such drugs to cases in which there was veterinarian oversight.

In December 2013, CVM issued Guidance for Industry #213, which presented information to drug sponsors to help them voluntarily remove growth promotion indications from the labels on antimicrobial drugs. The guidance asked the sponsors to respond within 3 months about their intentions concerning production claims.

Specifically, FDA asked affected sponsors to notify the agency in writing within three months, or by March 12, 2014, of their intent to engage with FDA as defined in Guidance for Industry (GFI) #213.

The number of affected sponsors is 26, and all 26 have confirmed in writing their intent to engage with FDA as defined in Guidance #213. These sponsors hold 100 percent of the applications affected by Guidance #213.

Antimicrobial drugs were largely approved as over-the-counter drugs until 1996 and used either in feed or water. However, by the mid-1990s, science had improved to provide more information about the potential for the development of resistance from the use of those drugs. Since 1996, as provided in ADAA, antimicrobial drugs for feed use were also approved as Veterinary Feed Directive (VFD) drugs.

FDA believes that antimicrobial drugs play an important role in helping to protect the health of animals. But to avoid the development of resistance, the use of certain antimicrobials should be controlled by veterinarians, who have the scientific and clinical training to know when to limit antimicrobial use. The way to give veterinarians a role in deciding when antimicrobial use is appropriate is to eliminate the over-the-counter

marketing status of certain drugs and instead make them Rx or VFD use only, which is FDA's goal under Guidance #213. To implement Guidance #213, FDA realizes that it must improve the VFD process, which is discussed in the next project (A4).

Project A4. Late in 2013, FDA proposed significant changes in its rules applying to Veterinary Feed Directive (VFD) drugs. CVM continues to gather information and comments from stakeholders concerning changes in the regulations applying to VFD drugs. The comment period closed in March 2014, and CVM is currently reviewing the comments.

VFD drugs are approved for use in animal feed and can be used only under the supervision of a veterinarian. The VFD regulation, which became effective in 2001, established requirements related to the distribution and use of VFD drugs and animal feeds that contain such drugs.

One of the proposed key changes would be to the definition of a veterinarian-client-patient relationship. More information about that change is available at http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/default.htm.

The proposed changes were based in large part on recommendations and comments CVM received from an Advance Notice of Proposed Rulemaking, issued in 2010. CVM had received a number of informal general comments that characterize the current VFD process as being overly burdensome. In addition, CVM had heard from the industry about concerns that the process, in its current form, will become particularly problematic to administer in the future as the number of approved VFD drugs increases. When veterinary oversight of a medicated feed is determined to be necessary, it is critically important that such oversight be facilitated through an efficient VFD process.

Component B – Limits for Feed Hazards

Feed contamination can result from exposure of feed ingredients and mixed feed to environmental, agricultural, industrial, or other sources of hazards, at any stage of the feed production continuum – from pre-harvest activities through feed manufacture, storage, and transportation and continuing to on-farm feeding practices. The likelihood of a feed hazard reaching levels that lead to safety concerns depends on a multitude of factors. For example, feed hazards initially present in feed ingredients and mixed feed at levels below the level of concern can be inadvertently increased to toxic or deleterious levels by certain harvesting and manufacturing practices or storage or transportation conditions. For example, if corn is not stored appropriately, aflatoxin can be produced by fungi present on the corn and reach levels that are toxic to animals. Feed hazards could also be added deliberately to feed to cause serious adverse animal and human health and economic problems.

The Agency uses several approaches to help eliminate or control risks from feed hazards in regulated feed products, such as establishing regulatory or guidance limits for feed

hazards, prescribing preventive controls for regulated feed products, establishing tolerances through the food additive petition process, or relying on a case-by-case review by experts to determine whether specific contamination incidents are unsafe. Limits can take the form of tolerances, which are regulations having the force of law; action levels, which are informal judgments about the levels at which consumers may be safely exposed to feed hazards; regulatory limits, which identify levels of feed hazards at which feed ingredients and mixed feed are considered to be adulterated; and guidance levels, which represent the Agency's current policy to industry. Once limits are created and understood, it becomes easier to control the risks from the feed hazards by product- or process-based approaches, either initiated by industry or required by a Federal or State regulation.

The Agency has established limits for some of the more obvious feed hazards, but it has no process for systemically assessing the need for limits for other known or newly recognized feed hazards. This AFSS component includes the processes by which FDA assesses the need to establish regulatory or guidance limits, and prioritizes the needs based on the level of risk posed to animal or human health.

When the Agency decides that limits for feed hazards need to be established, that decision calls for the development of a rapid, inexpensive, and reliable feed ingredient and mixed feed monitoring test kits that then must be validated, and made available for use by industry and government. FDA has developed an internal standard operating procedure (SOP) for ensuring that methods of detecting a feed hazard in feed ingredients and or/mixed feed are available for use by FDA and other government agencies and the regulated industry. This SOP, which is available at http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/PoliciesProceduresManual/UCM046777.pdf, places an emphasis on ensuring that such methods are capable of meeting the Agency's limits using established criteria. Appendix II contains the Agency's current procedures for establishing limits for feed hazards in feed and feed ingredients. The same appendix also contains references for the limits established by FDA, the U.S. Environmental Protection Agency, AAFCO, Codex Alimentarius Commission, the Food and Agricultural Organization, and the World Health Organization.

Current Project Work

Project B1. Not all feed hazards carry the same risk for adverse consequences to animal and/or human health. The Agency needs a systematic process whereby it can distinguish among feed hazards based on the risks they pose to animal or human health.

As indicated previously, the Agency is planning to rely on risk assessments when making decisions about feed safety. The use of risk concepts is not new for the Agency, as we routinely estimate public health impact in deciding where to focus regulatory effort. However, what will be new is the systematic application of a risk-ranking method that ranks all identified feed hazards in relation to each other. The risk-ranking method being developed by the Agency will try to account for the whole feed manufacturing

continuum: from feed hazards present in incoming materials or feed ingredients (product-related risks); through the potential for modulation of these feed hazards – increase, decrease, or remain at the same level – by manufacturing processes (process-related risks); to how the feed ingredients and mixed feed are handled by feed manufacturers, transporters, and on-farm mixers (facility-related risks), for instance. Public meetings were held on September 12, 2006 (http://www.fda.gov/AnimalVeterinary/SafetyHealth/AnimalFeedSafetySystemAFSS/ucm053828.htm), May 22, 2007 (http://www.fda.gov/animalveterinary/safetyhealth/animalfeedsafetysystemafss/ucm054979.htm), and May 14, 2008 (http://www.fda.gov/AnimalVeterinary/SafetyHealth/AnimalFeedSafetySystemAFSS/ucm053825.htm). At these meetings, CVM made presentations about risk, risk-ranking, potential feed hazards, and health consequence and exposure scoring for chemical and microbiological feed hazards. A critical part of the risk-ranking method development is the population of the data cells with sufficient feed hazard data to ensure a robust test. FDA has cooperative agreements with a dozen States under which feed hazard data will be collected by these States and then shared with the Agency. Further, data generated by FDA under its Feed Contamination Compliance Program are being used, as are data collected through Health Hazard Evaluations associated with feed contamination occurrences. Once the "model" is running, experts will be asked to conduct an evaluation to confirm the validity of the model's assumptions and findings.

Component C – Production, Storage, and Distribution of Safe Feed Ingredients and Mixed Feed

Prevention is the cornerstone of any hazard control plans. For example, a plan could include the implementation of written procedures calling for testing incoming loads of feed ingredients that are known to be susceptible to the molds that produce aflatoxin, thus ensuring that aflatoxins are not present at unsafe levels. Established verification procedures in a feed safety system are used to confirm that products are safe and that they comply with regulatory requirements.

The FDCA provides FDA with the statutory authority to regulate the manufacture, packaging, storage, and use of animal drugs, including Type A medicated articles and medicated feed, to ensure conformity with the current Good Manufacturing Practice regulations. Regulations mandating and specifying medicated feed current Good Manufacturing Practices are located in Title 21 of the *Code of Federal Regulations* at 21 CFR 225. The regulations for Type A medicated articles are located in 21 CFR 226. Complete citations of the regulations are listed in Appendix III.

Good manufacturing practices provide a systematic approach for ensuring feed safety through the identification and use of appropriate controls during the manufacturing, packaging, storing, and distributing of feed ingredients and mixed feed, and they are useful beyond animal drugs. The AFSS Team's review of the U.S. feed safety system conducted prior to passage of the FSMA legislation found that the United States lacked

certain baseline requirements for producing safe animal food, including Federal Current Good Manufacturing Practice regulations.

The proposed FSMA rule calls for animal food and ingredient producers to establish good manufacturing practices addressing manufacturing, processing, packing, and holding animal food. It also would establish hazard analysis and risk-based preventive controls for food for animals for some facilities. These measures will provide a greater assurance that animal food is safe and will not cause illness or injury to animals or humans consuming animal food products.

Current Project Work

Project C1. Under FSMA, CVM is developing a preventive control rule that would apply to feed and feed ingredient manufacturers. A proposed rule was published for comment on October 29, 2013. The comment period, which was extended once, closed on March 31, 2014. More than 2,100 comments were submitted from pet owners, pet food manufacturers, feed manufacturers, food companies, feed and food trade associations, law firms, and States, to name a few submitters.

Project C2. To ensure the preventive controls are understood, the Agency is developing several guidance documents. One guidance document would help the regulated industry develop feed safety plans, with specific emphasis on hazard identification and control methods. A second guidance document will help the industry comply with the other segments of the preventive control regulations. Most, in fact nearly all, farms that produce and store feed will not be required to comply with the animal food preventive control regulations. The farms that will be required to comply are those required to register with FDA as part of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002. We expect to write guidance for these animal feeders to help them make sure that their animals' health is not adversely affected by feed hazards and that human food provided by their animals does not compromise human health (see Project F1).

Component D – Reporting of Unsafe Feed

The surveillance programs conducted by the FDA and State feed control offices generate data about unsafe feed. Surveillance by the feed industry, animal producers, practicing veterinarians, and the public can be an important source of additional information should any of these groups learn about feed that had been adulterated.

The FDAAA directed the FDA to establish a "Reportable Food Registry" through which instances of "reportable food," including human food and animal feed, are reported via an electronic portal to FDA. Reports of reportable foods are made by food and feed establishments that have registered with FDA as required by Section 415(a) of the FDCA, and by Federal, State, and local public health officials. The Agency is charged to include in the Reportable Food Registry only those reports that describe cases in which the responsible party has determined the reportable food has a reasonable probability of

causing serious health consequences or death to humans or animals. In the *Federal Register* of September 9, 2009, FDA's Center for Food Safety and Applied Nutrition and CVM announced the availability of a Reportable Food Registry guidance document that provides guidance to the industry about complying with the Reportable Food Registry requirements. Public workshops were held on July 25, 2009 (College Park, MD), August 5, 2009 (Chicago, IL), and August 25, 2009 (Oakland, CA), to explain the intent of the guidance in more detail. The Reportable Food Registry and guidance apply to all FDA-regulated categories of human foods (except dietary supplements and infant formula) and animal feeds.

In May 2010, FDA launched the Safety Reporting Portal, which allows responsible parties to report reportable foods directly to FDA's Reportable Food Registry. The Safety Reporting Portal is accessed from the FDA Web site.

The FDAAA also required that FDA establish a Pet Food Early Warning Surveillance System to detect adverse events associated with pet food. Consumer complaints are the primary source of surveillance data for the Pet Food Early Warning Surveillance System. Consumer complaint coordinators in each of FDA's District Offices collect complaints through telephone calls from consumers in their district. In addition providing a place to send Reportable Food Registry reports, the Safety Reporting Portal offers consumers an additional mechanism to report their pet food complaint to the FDA. Within days of opening the Safety Reporting Portal for pet food complaints, reports from veterinarians diagnosing thiamine deficiency in cats enabled FDA to facilitate a rapid recall by the manufacturer of a cat food that lacked adequate levels of thiamine. In addition, the medical information uploaded to the Safety Reporting Portal by the veterinarians was beneficial to FDA scientists classifying the recall of the affected cat food product.

Consumer complaints and Reportable Food Registry reports collected through the Safety Reporting Portal have proved that the Portal is a valuable new surveillance tool for the Pet Food Early Warning Surveillance System. The Portal has increased FDA's ability to identify animal feed problems earlier and respond more rapidly.

In March 2014, CVM enhanced its animal feed reporting systems, by adding to the pet food safety portal and the reportable food registry a Web site for the public to report problems related to livestock animal feed. The Livestock Food Reporting portal accepts reports about foods made for species considered to be livestock, including but not limited to, horses, cattle, swine, poultry and fish. Anyone, including veterinarians and livestock producers, with concerns about the safety of an animal feed can file a report.

The Livestock Food Reporting portal is the latest addition to the Safety Reporting Portal, an online system designed to streamline the process of reporting product safety issues to the FDA and the National Institutes of Health. Animal feed manufacturers, distributors, retailers and public health officials at the Federal, State, and local level should continue to use the Reportable Food section of the Safety Reporting Portal. The Portal can be found here: http://www.safetyreporting.hhs.gov/.

Beginning in 2009, the Partnership for Food Protection, a collaboration of Federal, State, and local governments with roles in protecting the food supply and public health, started to develop a new system that will allow States and the Federal government to share information about contaminated pet food products. The system, called the Pet Event Tracking Network, or PETNet, was officially launched on August 1, 2011. In PETNet, information is shared over a secure information network with State and Federal regulatory agencies with jurisdiction over pet food products. PETNet's goal is to disseminate information to regulators – typically States – who are in the best position to take quick action to protect the health of pets as soon as the information becomes available to FDA. (PETNet is for government use only and is not accessible by the public.)

Current Project Work

Project D1. Feed mills licensed by FDA to use Type A medicated feed articles are required by 21 CFR 510.301 to submit records and reports to FDA concerning clinical and other experience with the types of medicated feeds (Type A) that the licensed permits them to use. The regulation does not require feed establishments and animal drug manufacturers to submit the type of information about the safety of marketed feed that the Agency could use to make more informed decisions.

The Agency believes that the regulations in 21 CFR 510.301 should be updated and is planning to solicit comments via a *Federal Register* notice. The proposal will provide technical changes to clarify the reporting requirements of licensed feed manufacturers.

Project D2. In late 2010, CVM's Office of Research initiated a project, the Veterinary Laboratory Investigation and Response Network (Vet-LIRN), to collaborate with veterinary diagnostic laboratories to exchange scientific information, build laboratory capacity, and train scientists. The overall goal for CVM is for participating laboratories to be ready, willing, and able to help investigate potential problems with animal feed and animal drugs. By the beginning of 2014, the initiative had expanded from the 16 original member laboratories to 34 member laboratories. The network should, among other things, provide the means for rapid response to reports of animal injury. During its first year, Vet-LIRN conducted 5 in-depth cases investigations and multiple case evaluations. By the beginning of 2014, it had conducted 23 in-depth investigations, as well as multiple case evaluations. Vet-LIRN has also been heavily involved in CVM's investigation of the illness in dogs associated with eating pet jerky treats. Since 2011, Vet-LIRN has conducted more than 1,000 tests on jerky pet treat samples. At the same time, Vet-LIRN staff has managed the work of 11 laboratories doing research to harmonize a method for detecting *Salmonella* in pet fecal samples to evaluate the consequences of contaminated feed on background infection prevalence and to facilitate case investigations.

In addition, the Vet-LIRN system has been used to conduct multiple network-wide chemical and microbial proficiency tests to demonstrate that the participating laboratories provide accurate and meaningful testing data to FDA.

Component E – Regulatory Oversight

The primary purpose of regulatory oversight is to determine an establishment's or a product's degree of compliance with applicable regulations. The term regulatory oversight should be considered in its broadest view, covering, for example, the review of labeling done at the regulator's site of business or on the firm's Web site, or an on-site inspection of the establishment's manufacturing facility. Surveillance inspections are conducted to determine whether an establishment is in compliance with the regulations and the operation is adequately controlled. Compliance inspections are conducted to evaluate an establishment's compliance with the provisions of the regulations and to document inspectional observations supporting possible enforcement action.

Because the majority of inspections of feed manufacturing and distribution establishments – which fall under the jurisdiction of FDA – are done by State agencies using Federal or State authority, FDA's strong working relationship with State counterparts will continue to be a significant component of the AFSS. A scientific risk-based approach will be utilized to improve the Agency's ability to prioritize and allocate inspection resources by targeting establishments, facilities, products, and processes posing the greatest risks to animal or human health.

A new approach the Agency is allowing is the use of third-party certification. A guidance document, entitled Voluntary Third-Party Certification Programs for Foods and Feeds (http://www.fda.gov/regulatoryinformation/guidances/ucm125431.htm), was released in January 2009 and provides more information on this topic. While third-party certification programs are not intended to take the place of inspections performed by a regulatory agency, if a firm is participating and compliant in a recognized third-party program, the firm is likely at lower risk for problems than a firm that is not participating.

Regulatory compliance efforts often rely on voluntary compliance with the law and regulations. When voluntary compliance and education are unsuccessful, the Agency has other options, such as Untitled Letters, Warning Letters, informal meetings, mediation, civil penalties, administrative hearings, injunctions, seizures, and criminal prosecutions. Enforcement action would not be taken based on information from third-party certifiers; however, an inspection by a regulatory agency could be used to follow-up and document violations for enforcement action. See Appendix IV to find more information about regulatory oversight.

FDA's current feed safety program does not always include adequate attention to each segment of the industry, such as those responsible for the production, distribution, and use of feed. Regulatory oversight has focused principally on the commercial medicated feed industry and large integrated operations, even though there has been a major shift in the industry to more production on the farm. Some on-farm operations are making more feed than most commercial feed companies. CVM is considering how to improve oversight of the on-farm feed producers and other segments of the feed industry, such as transportation companies, importers, and warehouse/storage facilities. Risk associated

with these segments will be assessed to determine where the Agency will focus its limited resources.

Current Project Work

Project E1. The FDA has collaborated with AAFCO to develop the Animal Feed Regulatory Program Standards (feed standards) for use by State programs responsible for the regulation of animal feed. FDA and AAFCO jointly announced the availability of the Program Standards in February 2014. Since that time, FDA has been developing the implementation program to encourage States to implement the feed standards and provide technical assistance during implementation. Implementation of the feed standards will promote uniformity and consistency among animal feed regulatory programs and provide a platform for mutual reliance within a national integrated food safety system. The standards do not apply to animal feed manufacturers, but instead were developed for and intended to be implemented by animal feed regulatory programs. The Program Standards are available on the FDA Web site at: http://www.fda.gov/ForFederalStateandLocalOfficials/AnimalFeedRegulatoryProgramStandardsAFRPS/default.htm.

Project E2. Vehicles, including trucks and rail cars, used to transport feed have historically received limited inspectional scrutiny. Additionally, because these vehicles are frequently owned and operated by someone other than the feed manufacturer, the feed manufacturer often lacks much control of the vehicle, as well. The combination of limited inspection by regulators and lack of control by the feed manufacturer creates a situation in which efforts to prevent cross-contamination might not be promoted or used.

In response, the Agency has begun rule-making to implement the Sanitary Food Transportation Act (SFTA) of 1990. Although originally delegated to the U.S. Department of Transportation, the authority was transferred to FDA and the U.S. Department of Agriculture in 2005. FDA published an Advance Notice of Proposed Rule-Making in the *Federal Register* on April 30, 2010, seeking comment from the public and industry on a series of questions regarding the transportation of food (including food for animals). The Food Safety Modernization Act (FSMA) required the Agency to implement the SFTA, which has given the rule-making process a new focus. To this end, the Agency published proposed rules in the *Federal Register* on February 5, 2014, with comments due by July 30, 2014. The rules under development are intended to minimize the opportunities for cross-contamination during transportation, and they will strengthen the Agency's ability to regulate the transportation of feed and feed ingredients. CVM is working with FDA's Center for Food Safety and Applied Nutrition and Office of Foods and Veterinary Medicine on this issue.

Project E3. All imported products are required to meet the same standards as domestic goods. Feed imports have increased dramatically, but without a significant shift in the way the Agency conducts its oversight – until recently.

In September 2007, the President's Interagency Working Group on Import Safety reported the burdens facing border officials caused by the growth of imports and by an increased focus on security. The report noted that these officials must manage larger volumes of imports from countries that often have a less-developed regulatory system. In addition, border officials must consider more complex risk scenarios, use more sophisticated screenings and examinations, and employ new technologies to ensure product safety. The report made clear that a new Strategic Framework would be needed to ensure the safety of imported products that are consumed and used in the United States. The Agency is working on such strategic frameworks.

FSMA directed FDA to expand its management of imported food. FDA has a presence in many foreign countries that produce and export food to the U.S.; however, the ability of the U.S. to establish a presence is limited by available resources and access restrictions. The resource limits of the Agency require us to rely upon stakeholders and partnerships. FSMA has provided FDA with the authority to establish requirements for importers of food and feed. The Agency's relationships with regulatory partners and industry stakeholders will be enhanced through foreign supplier verification programs and the accreditation of third-party auditors. FDA published a proposed Foreign Supplier Verification Program rule on July 29, 2013, and a proposed rule on the Accreditation of Third-Party Auditors on that same day. FSMA also requires the establishment of a voluntary qualified importer program. Further, the latest prior notice guidance (Draft Guidance for Industry: Prior Notice of Imported Food Questions and Answers [Edition 3]) has been made available for public comment, with a comment period scheduled to close on in May 2014. The revisions were made largely to reflect two new rules, one published in 2008 that requires prior notice for food, including animal feed, and one in 2013 that requires that FDA be advised if a food was not permitted entry by another country.

Project E4. CVM and FDA's Minneapolis District (the District includes the States of Wisconsin, Minnesota, North Dakota, and South Dakota, as well as FDA's District Office) are participating in a pilot project for assigning inspections based on risk factors. The participants are presently identifying and ranking health-related risk factors, which will be used to rank the feed facilities in each State within the District as high-risk and low-risk. All high-risk facilities with be inspected by Federal or State inspectors. Low-risk facilities will have less frequent inspections. The pilot is expected to run for 3 years. After gaining experience from the first year of inspections, the program developers were able to reduce the number of risk-ranking criteria, to simplify the process, and to modify the weights assigned to each criterion used to determine the potential for impacting animal or human health.

COMPONENT F – Education and Outreach

For a comprehensive regulatory approach to be successful, cooperation between FDA and State regulatory programs will be essential. In addition, the timely development and distribution of educational materials and guidance documents for the feed companies and producers will be necessary as portions of the AFSS and FSMA are implemented. It is

critically important to have program and inspection staff well trained in all facets of the Agency's feed safety program and an industry that knows what is required for compliance with FDA rules in order to prepare, distribute, and use feeds in a safe manner. However, such education and outreach initiatives need to be timely, informative, understandable, and available to those needing the information.

The AFSS places heavy emphasis on developing and implementing education and outreach programs, which it uses in conjunction with inspection and enforcement activities to bring about compliance with safe feed rules and policies.

The introduction of a new regulatory feed program or the modification of an existing one requires training to ensure that FDA and State personnel understand the new or modified program and that they are capable of carrying out the program's mandate. Furthermore, it is essential for the Agency to prepare and distribute outreach materials to aid the industry in achieving compliance, because voluntary compliance by industry means less compliance effort by regulatory agencies.

One key to success with these outreach and education efforts is timing. The information must reach the users when they need it.

Delivering the message using formats familiar to the industry and other stakeholders is another key to success. The Team made a significant step in this regard during 2013 when it launched a new Web page that was designed to be easy to find and use. The Team gathered links to all pertinent feed safety information that is scattered throughout the FDA Web site and placed those links a single page: www.FDA.gov/SafeFeed. Further, the Team arranged the information based on a user's needs. For example, the page has a navigational button for anyone who wants more information about feed ingredients, or about manufacturing feed. Regulatory information is on that page, too. And, to make the information even more available, the page was developed so that it will properly display on a mobile device as well as on a computer screen. Feed manufacturers and regulators can access information without having to return to an office computer to look it up.

Also, CVM has developed a Web-based system that housed the most recently approved Blue Bird labels for Type B and C medicated feeds. The system, which was made available in June 2009 for a number of approved drugs, provides the medicated feed industry with the best opportunity to ensure that accurate labeling is developed and used. In addition, by using resources available on the Internet, licensed medicated feed mills will be operating in compliance with the requirement of 21 CFR 515.10 by having in their possession current approved Type B or Type C medicated feed labeling before they receive Type A medicated articles. CVM is continuing to add new Blue Bird labels to the system.

Current Project Work

Project F1. Assessing and controlling feed hazards must occur along the entire feed continuum, including the use (the feeding) of feedstuffs on-farm. The Agency's feed safety program activities have dealt mainly with commercial feed establishments. However, on-farm establishments, which represent the last location of feed before it is fed to food-producing animals, have received limited FDA and State oversight.

While no regulations are being considered at this time to address the safe feeding of food-producing animals, we have prepared draft guidance to assist animal feeders in ensuring that their on-farm practices are consistent with maintaining, storing, and feeding safe feed**.** This guidance will be available for public comment when completed. Furthermore, we intend to partner with our stakeholders in the development and dissemination of materials that reduce the guidance to practical terms.

Project F2. It has been several decades since FDA feed labeling regulations, including those for pet food, have been updated. On the other hand, the AAFCO model pet food regulations have been amended nearly each year since they were adopted by the AAFCO membership in 1967. Because the AAFCO regulations were aimed to keep pace with industry desires and public interests, they became the de facto accepted standard, even though they have not been adopted by every State. The public, pet food industry, government agencies, and AAFCO agree that current Federal pet food labeling can be improved to provide more meaningful information to pet owners about the nutrition and safe use of the food they purchase for their pets.

FDAAA also requires updated labeling standards for pet food. Congress is requiring a regulation that includes standards for nutritional and ingredient information on the label. The Agency established a docket (#2007-N-0442) about this topic. A Public Meeting was held on May 13, 2008, to receive comments from interested parties. A proposed regulation is being drafted for public comment.

Project F3. AFSS Team members have taken advantage of the general availability of the Internet by placing videos about feed safety and U.S. feed standards on it, thus making the information available to international as well as domestic audiences. The information is available at any time to anyone with a computer and an Internet connection.

In 2010, the AFSS Team created its first video, which highlighted various safe animal feed and pet food principles. The 5-minute video highlighted the role of feed manufacturers and animal feeders in ensuring the safety of food derived from animals. The video, "Safe Animal Feed," is available on the FDA's Web site and was also recorded on disks for distribution at trade shows and other meetings.

Since that video was produced, the Team has also produced others about: how pet food is regulated ("FDA and Pet Food"), how to safely handle pet food in the home ("Pet Food and Treats in your Home"), and (two videos) about medicated feed labels ("Helping Animal Producers Understand Medicated Feed Labels," and "Medicated Feed Rules for

Animal Feed Manufacturers"). The Team intends to make additional videos that will make the rules and policies of safe animal feed easily understood by all audiences.

COMPONENT G – Research

CVM's Office of Research is charged with conducting research in support of CVM areas of responsibility, such as ensuring the safety of animal feed in this country. The Office of Research, which is located in Laurel, MD on a 167-acre plot of land, has facilities to house several types of animals and fish. The Office of Research is a multidisciplinary organization with a scientific staff trained to work on a wide array of issues. The three main areas of work are: analytical research for compounds that pose a health risk if found in animal tissue or animal feed; applied and basic research in animal health and medicine in support of current and evolving regulatory issues; and applied and basic research regarding microorganisms potentially harmful to animals and humans. More information on the Office of Research is available on the CVM Web site.

Current Project Work

Project G1. Antibiotics (e.g., penicillin and virginiamycin) are being used to prevent unwanted bacterial growth in the fermentation of corn and other substrates for ethanol production. The mash or distillers grains derived as a byproduct of the ethanol fermentation process have been found to contain low level residues of these antibiotics. Research is being conducted to determine whether the level of antibiotics found in distillers grains confer antibiotic resistance in pathogenic strains of bacteria. A poster was presented on the initial phase of the research[†]. Additional research is proceeding on virginiamycin, penicillin and erythromycin.

Project G2. The Office of Research has a study underway with a goal of combining technology available from recent advances in nanotechnology and genomics to develop a field-operable, handheld biosensor device for rapid, sensitive, specific, and affordable verification of species in FDA-regulated products. The objectives of this study are to: (1) verify the specificity of DNA probes for targeting the various DNA signatures of DNA-targeted ruminant species for a biosensor format; (2) optimize the sample processing method for DNA extraction of FDA-regulated products for a biosensor format and field operability; (3) synthesize bio-conjugated nanoparticles for effective extraction, hybridization, and detection of target DNA signatures; and, (4) test the biosensor in the field and at selected inspection sites.

An example of a specific research project underway is work regarding Porcine Epidemic Diarrhea virus (PEDv). PEDv outbreaks in the USA have caused 60-100 percent mortality in suckling pigs and mild to severe diarrhea in pigs of all ages. Spread of this virus mainly occurs directly through infected pigs and indirectly through virus-

[†] Karen Blickenstaff, Faiza Benahmed, Sonay Bodeis-Jones, Marla Luther, Linda Benjamin & Mark Rasmussen, *Impact of Low Level Antimicrobial Residues in Distillers Grains.* Abstract at Poster session of Symposium on Biotechnology for Fuel and Chemicals, New Orleans, LA. May 2, 2012

contaminated fomites and via transportation trucks. However, there were some concerns that the virus can be spread via feed. To address this possibility, the Office of Research has developed a method to extract the virus from plasma and is optimizing the method to determine if the method is suitable for feed.

Project G3. Current FDA regulatory methods for determining selenium levels in feeds are obsolete. Incorporation of the analysis for selenium into multi-elemental analysis will allow FDA's Office of Regulatory Affairs and State regulatory laboratories to more efficiently test feeds for selenium. A method exists in the FDA Elemental Analysis Manual for quantifying several elements by inductively coupled plasma-mass spectrometry (ICP-MS) with microwave assisted digestion (including arsenic [As], cadmium [Cd], chromium [Cr], lead [Pb], mercury [Hg] and others) in food and related products. The proposed research will expand the ICP-MS method to include selenium in animal feed along with method-specific figures of merit (LOD, LOQ, etc.).

Appendix I

Processes:

1. Food Additive Petition; FDA (21 CFR 571)
2. New Animal Drug Application (NADA); FDA (21 CFR 514)
3. Generally Recognized As Safe (GRAS) Petition - FDA (21 CFR 570); GRAS Notification proposed rule 62 FR 18938 (CFSAN is accepting notifications now)
4. Color Additive Petition; FDA (CFSAN) (21 CFR 71)
5. AAFCO Ingredient Definition Process (*2014 Official Publication; pp 337 - 341*)
6. Common or Usual Name Recognized by the Secretary/Director/ Commissioner of Agriculture; FDA and AAFCO (21 CFR 502 and AAFCO OP)
7. Bioengineered Plants – CFSAN Guidance document, October 1997 - consultation process with FDA
8. Drugs, Biologics, and Medical Devices Derived From Bioengineered Plants for Use in Humans and Animals (FDA Draft Guidance #153)
9. AAFCO Feed Labeling Model Regulations and Guides (food-producing animals and pet animals) – 2014 Official Publication

Ingredient/Additive Listings:

1. Food Additives Permitted in Feed and Drinking Water for Animals -21 CFR 573
2. New Animal Drugs for Use in Animal Feeds - 21 CFR 558
3. Generally Recognized of Safe (GRAS) Substances - 21 CFR 582 & 584
4. Color Additives - 21 CFR 73 & 74
5. Feed Ingredient Definitions - AAFCO 2014 OP (pp 342 – 454)
6. Substances Prohibited for Use in Food and Feed (21 CFR 589)
7. Bioengineered Plants - CFSAN home page http://www.fda.gov/Food/default.htm and 9 CFR 340
8. Animal Food Labeling - 21 CFR 501, 21 CFR 201

9. Compliance Policy Guide 7126.08 - Common or Usual Names for Animal Feed Ingredients
10. Pesticides Approved by EPA for Use in Feed and on Crops - 40 CFR 180
11. Biologic Products Approved by USDA for Use in Animal Feed - 9 CFR 101-123
12. Indirect Food Additives Resulting from Packaging Materials for Animal and Pet Food – 21 CFR 181 and 174 through 179 as cited by 21 CFR 570.13 and 570.14

Appendix II

Processes: Procedures for establishing limits for contaminants in feed and feed ingredients include the following:

1. Setting tolerances, action levels and regulatory limits for feed contaminants are described in 21 CFR 509.4 through 509.7.
2. Setting guidance levels are described in FDA's Good Guidance Practices Regulations, 21 CFR 10.115.

Contaminant Limits: FDA has established Limits on contaminants in food and feed,

1. Aflatoxin action levels (FDA's "Compliance Policy Guide" (CPG) 683.100);
2. Pesticide tolerances (EPA's *Code of Federal Regulations* (CFR), Title 40, Part 186 and FDA's CPG 575.100);
3. Pesticide action levels (FDA's CPG 575.100 & *Federal Register* (FR), Vol. 55, No. 74; April 17, 1990);
4. Temporary tolerances for PCB's (FDA's 21 CFR 509.30);
5. Guidance levels for Fumonisin (FDA's Guidance for Industry #112);
6. Guidance for Industry and FDA: Advisory Levels for Deoxynivalenol (DON) in Finished Wheat Products for Human Consumption and Grains and Grain By-Products used for Animal Feed;
7. Substances prohibited from use in animal food or feed (FDA's 21 CFR 589);
8. Tolerances established for drugs in food (FDA's 21 CFR 556);
9. Guidance levels for trace mineral contaminants (AAFCO's 2014 Official Publication; pg 302);
10. Salmonella in Food for Animals (FDA's CPG.690.800); and,
11. Regulatory limit for Salmonella (FDA's 21 CFR 500.35); and
12. Draft Guidance for Industry: Testing for Salmonella Species in Human Foods and Direct-Human Contact Animal Foods; Availability (*Federal Register*, Vol. 76, No. 56, Wednesday, March 23, 2011, 16425

Appendix III

Operations/Manufacturing Process Listings:

1. Medicated Feed cGMPs (21 CFR 225)
2. Type A Medicated Article cGMPs (21 CFR 226)
3. AAFCO Feed Manufacturing Regulations 2014 OP pp 210 – 219

4. Low acid canned food regulations (21 CFR 500.23)
5. Codex Code of Practice for Good Animal Feeding http://www.codexalimentarius.org/search-results/?cx=018170620143701104933%3Ai-zresgmxec&cof=FORID%3A11&q=Codex+Code+of+Practice+for+Good+Animal+Feeding&siteurl=http%3A%2F%2Fwww.codexalimentarius.org%2F
6. HACCP; (seafood 21 CFR 123 and juice 21 CFR 120)
7. SSOP (21 CFR 120.6 and 123.11)

Appendix IV

Inspection and Enforcement Descriptions: Inspections (FD&C Act Subchapter 701)

1. Enforcement (FD&C Act Subchapter 704-706; IOM Chapter 2) http://www.fda.gov/ICECI/Inspections/IOM/default.htm (under Chapter 7)
2. Federal-State Cooperation (IOM Chapter 3) http://www.fda.gov/ICECI/Inspections/IOM/default.htm (under Chapter 3)
3. Regulatory Procedures Manual http://www.fda.gov/ora/compliance_ref/rpm/default.htm
5. Audits conducted by FDA of State inspections http://www.fda.gov/ForFederalStateandLocalOfficials/PartnershipsContracts/StateContracts/AuditReportsonStateFoodContractInspections/default.htm

Inspection and Enforcement Listings:

1. Administrative actions refer to 21 CFR, particularly parts 12, 511, 514, and 571 FDA and AAFCO Enforcement Guidelines (CVM Policy and Procedure Guide 1240.3600) (http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/PoliciesProceduresManual/ucm046222.htm
2. Federal and State Audits (FDA Field Management Directive #76) http://www.fda.gov/downloads/ICECI/Inspections/FieldManagementDirectives/UCM384257.pdf
3. Inspection priorities (BSE Compliance Plan 7371.009) http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/ComplianceEnforcement/UCM113437.pdf
4. FDA Compliance Program Guidance Manual, Program 7371.003 Feed Contaminant Program; http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/ComplianceEnforcement/ucm113409.pdf
5. FDA Compliance Program Guidance manual, Program 7371.004 Feed Manufacturing Compliance Program; http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/ComplianceEnforcement/ucm113430.pdf